Molecular Immunology 68 (2015) 2–5

Contents lists available at ScienceDirect

Molecular Immunology

journal homepage: www.elsevier.com/locate/molimm

Review

Moh Daha, a successful scientist with a strong personality, who loves to stimulate and support his colleagues

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ARTICLE INFO

Article history:
Received 27 April 2015
Received in revised form 6 June 2015
Accepted 8 June 2015

Keywords:
Complement
Kidney
Clinical immunology
Autoimmune diseases
Transplantation

ABSTRACT

Mohammed R. Daha is a successful and very productive scientist. He is internationally recognised for his expertise of Complement. In addition, he contributed to many other fields of Immunology, in particular Clinical Immunology within Internal Medicine. He did not only contribute to Nephrology and Transplantation, but also to Rheumatology, Infectious diseases and Pulmonology. He enjoyed teaching and he was also appreciated for his guidance of biomedical and clinical PhD's.

1. His curriculum vitae

Moh's career in Immunology started in 1969 when he came as a student to the research laboratory of the Dept of Nephrology of Leiden University. I had asked Johan Lugtenburg in the Dept of Biochemistry for a talented student to help me with my PhD study in experimental glomerulonephritis in rats. During that time Moh showed his excellent skills in protein chromatography. Since then our careers in Leiden University Medical Center (LUMC) ran parallel, until I retired in 1999. Moh retired 10 years later. Together we supplemented each other and covered a wide range of expertise in Nephropathology, Moh in the basic aspects and I on the clinical aspects of renal diseases. Moh graduated in 1970 in Biochemistry and acquired his PhD in 1973 with his thesis on the synthesis and degradation of glomerular basement membrane in rats with experimental glomerulonephritis (Fig. 1).

Experimental immunopathology was new in our Dept of Nephrology. As in most other departments of Nephrology the emphasis was on electrolyte metabolism. When the first kidney transplantation in the Netherlands was performed in 1966 in the LUMC, the chief of Nephrology Prof Jaap de Graeff decided to change course and focus research on Immunology. It became my and Moh's task to make that happen.

Immunology was still a young discipline in the sixties. The first International Congress of Immunology took place in 1971 in Washington DC. Immunology was until then a discipline dispersed over a great variety of medical disciplines and specialties. The introduction of immunofluorescence and histochemistry contributed to diagnostics in Pathology, immunoglobulin precipitation and electrophoresis was relevant for the detection of multiple myeloma in Haematology and the detection of immunoglobulin deficiencies in Paediatrics, Departments of Bacteriology and Infectious diseases were interested in the detection and measurements of specific antibodies. The role of cellular immunity was of great interest to transplantation physicians, but methods to measure it were lacking. Immune mediators were widely considered important, but too complicated to have clinical application. It was this latter field that Moh embarked on. In 1973 he received a postgraduate grant to study immune mediators at Harvard in the laboratory of Frank Austin, especially in the Immunobiology of Complement. Thanks to the training he received in Frank Austin's lab, from Frank but also from Doug Fearon and others, Moh acquired the capacity to analyse laboratory data critically and to follow rigorous lines of reasoning. After his return to Leiden in 1976 Moh pursued his interest in the basic and clinical aspects of Complement. He became an internationally known expert in this field. In addition, through his talent to understand medical processes and through his natural inclination to support others, he extended in the course of his career his expertise in the fields of, transplantation, infectious diseases, rheumatology and pulmonology. His broad expertise allowed him to contribute to many medical journals as a referee. He was on the scientific Boards of the Dutch Foundations for kidney disease, lung disease and rheumatology. He was on the Board of the Dutch Society for Immunology, later he was on the Board of the International

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http://dx.doi.org/10.1016/j.molimm.2015.06.007
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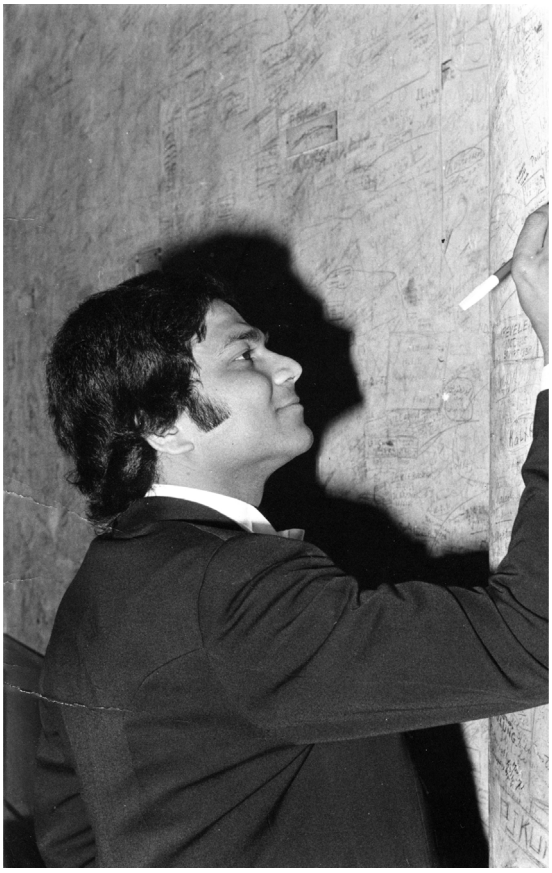

Fig. 1. Graduation ceremony. After the defence of his thesis in 1973, Moh puts his signature in the 'sweat-room' of the Academy building of the Leiden University.

Union of Immunological Societies (IUIS) to become Secretary General of the IUIS in 2001. He retired in 2009 and is still very active as an emeritus Professor at Leiden University (Fig. 2)

2. Moh's core scientific interests

After completing his PhD study, Moh started his studies at Harvard together with Doug Fearon on the immunobiology of Complement with the analysis of C3 Nephritic Factor, that we could isolate from a patient in our centre with membranoproliferative glomerulonephritis (Daha et al., 1977). It turned out that it was an autoimmune antibody that stabilises the alternative pathway C3 convertase. After his return to Leiden he continued to study the role of Complement in various diseases within the Dept of Nephrology. During his career he published clinical studies in collaboration with paediatricians on congenital complement deficiencies of C3,C5, C6, Properdin, the factors D, and H. Later in his career he focussed on the mannose binding lectin (MBL) pathway of Complement activation (Roos et al., 2003).

Fig. 2. Farewell ceremony. During his farewell ceremony in 2009, Moh vividly and enthusiastically explains the importance of the complement system.

Stimulated by the pivotal work of Frank Dixon in the sixties on the pathogenic effect of circulating antigen–antibody complexes (CIC), most research groups interested in the pathogenesis of glomerulonephritis focussed on these CIC. Moh and I developed a long and productive line of research on the composition and fate of these complexes in vitro and in vivo. Initially we focussed on the processing of these complexes by macrophages in vitro. Later studies were extended in the handling of preformed immune complexes in vivo (Kijlstra et al., 1979). These studies resulted in the preparation of stable immunoglobulin aggregates as surrogate immune complexes. We developed a method using radiolabelled immunoglobulin aggregates to measure the clearance rate of immune complexes, in healthy controls (Lobatto et al., 1987) and in patients with systemic lupus erythematosus (Lobatto et al., 1988; Halma et al., 1991).

Many assays became available to detect CIC in patients. A plethora of publications appeared on the clinical relevance of these assays for the detection of these CIC in patients with glomerulonephritis and systemic vasculitis. We were able to show CIC in patients with idiopathic leukocytoclastic vasculitis (Kauffmann et al., 1980a) and in vasculitis associated with bacterial endocarditis (Kauffmann et al., 1981). These studies gave also some surprising results. One of the first CIC assays was the C1q binding assay. This assay was shown to be positive in systemic lupus erythematosus (SLE), the prototype of an immune complex disease. Later it would turn out that SLE patients have autoimmune antibodies to C1q, that could bind in vitro to C1q in the absence of immune complexes. Moh was able to show that the level of these autoimmune antibodies to C1q correlate better with the severity of lupus nephritis than the level of antibodies directed against ds-DNA (Siegert et al., 1993). Another surprise involved a CIC assay using normal polymorphonuclear cells (PMNs) as a probe to detect CIC in patient sera. Fokko van der Woude in Groningen found that these PMNs also showed immunofluorescent staining in the absence of CIC. This resulted in the detection of anti-cytoplasmic antibodies (Van der Woude et al., 1985), later called anti-neutrophil cytoplasmic antibodies (ANCA). After Fokko van der Woude joined our group, a whole series of publication appeared about the association of ANCA and systemic vasculitis. Fokko and Moh standardised the ANCA assays between European laboratories (Hagen et al., 1993). This collaboration resulted in a very active European working group on vasculitis, that embarked on several multicenter trials on the treatment of ANCA-associated vasculitis.

Another spin-off of the immune complex line was that Moh developed an assay to detect IgA immune complexes. With this assay we were able to demonstrate circulating IgA immune complexes in sera of patients with Henoch-Schoenlein purpura (Kauffmann et al., 1980b) and IgA nephropathy (Valentijn et al., 1983). We showed that the mesangial IgA deposits consist of IgA1 subclass and components of the alternative pathway (Valentijn et al., 1984). We were also able to show an augmented bone marrow IgA1 response in these patients (Van den Wall Bake et al., 1989), but a deficient mucosal IgA1 response (de Fijter et al., 1996). Later Moh demonstrated also an important role of